babies continue to be born at home, with only the barest essentials in equipment and nursing service. Only an exceptional case will have received anything like proper repairs. Whether these people present a higher percentage of morbidity, we will have no way of demonstrating until new standards of evaluating morbidity become devised. At any rate it is safe to assume that most patients delivered at home will not be so well off as those delivered in a hospital. Perhaps a critical analysis and examination of every patient at six months would tell us just how effective our work is.

Exponents of the various forms of socialized medicine seem to want to do something for obstetrics. A bill submitted to the Assembly of the 1935 California Legislature hinted at such a discrimination. Let us suppose that movements like this did become nation-wide, and obstetrical departments, manned by full time, well-trained staffs, were subsidized and became available for moderate costs. Would these institutions compete with each other to give better service and decrease morbidity, or would they degenerate into a sort of minimal routine? Theoretically, it would seem so, but most doctors, as well as other people, need personal incentive.

Arrangements could easily be made for the centers of population, but the rural territory would be more difficult to accommodate. It would not be practical to scatter numerous maternity hospitals over the country, although it would be practical and possible to furnish capable consultants and nursing service from numerous stations placed at regular intervals over each state, and not compel the general practitioner to wade into situations for which he is not qualified.

It has been proposed that a direct cash repayment be made by the federal government to each mother for all, or a certain portion of money expended for hospitalization or for nursing care. Some countries reward each mother with a fixed sum of money. When this money is actually used for intrapartum and postpartum attentions, it is a definite contribution toward the reduction of maternal morbidity.

IN CONCLUSION

In conclusion, I will simply emphasize the need for more adequate and more informative standards with which to measure our unsatisfactory results. When these are tabulated, greater attention can be directed to the details responsible for the unfavorable percentages. After a certain amount of urging, we hope the hospitals will provide more complete delivery-room facilities, and even skilled obstetrical anesthetists. The antepartum and the more remote postpartum management will continue to be the responsibility of the individual obstetrician. These will require efficient and persistent educational propaganda, for the physician as well as the patient, such as is so effectively instituted for antepartum care.

1680 North Vine Street.

GENERAL PARESIS—THE USE OF DRUGS IN ITS TREATMENT*

By EUGENE ZISKIND, M. D.
Los Angeles

DISCUSSION *by George S. Johnson, M.D., San Francisco; Stanley O. Chambers, M.D., Los Angeles; Clifford W. Mack, M.D., Livermore; Samuel D. Ingham, M.D., Los Angeles.*

SINCE our experience in the clinic for neurosyphilis at the Los Angeles County General Hospital has not been reduced to a statistical basis, we have limited ourselves, in this paper, largely to conclusions drawn from a survey of the recent literature. The inadequacy of the routine antisyphilitic remedies (arsphenamins and heavy metals) for general paresis is universally acknowledged. Hence, in the treatment of this disease, one thinks chiefly in terms of tryparsamid or some form of fever therapy.

IMPORTANCE OF ARSPHENAMINS AND HEAVY METALS IN NEUROSYPHILIS

Nevertheless, it may not be amiss to emphasize the importance of the arsphenamins and heavy metals in neurosyphilis. Tryparsamid is not spirocheticidal. After malaria, although spirochetes can no longer, as a rule, be demonstrated in the brains of paretics at necropsy, active lesions in other organs may still be flourishing.[1] Hence, all patients, whether treated by fever-producing agents or tryparsamid, should have additional treatment with the classic antiluetic drugs. Probably one is never justified in using the latter measures at the outset of the treatment. Much valuable time may be lost in this manner, because arsphenamins and the heavy metals do not check the progression of the cerebral pathology.

BISMUTH THERAPY

A word should be said as to the rôle of bismuth in the treatment of neurosyphilis. The work of Hanzlik, Mehrtens, and their co-workers,[2] has definitely established the increased penetrability of iodobismitol into the central nervous system. But bismuth is only mildly spirocheticidal, and nowhere have results with this drug indicated that it is a substitute for tryparsamid or malaria. Its value as an adjuvant to therapy, and its superiority to mercury, are unquestioned.

TRYPARSAMID AND MALARIAL THERAPY

The use of drugs in the treatment of paresis centers about tryparsamid. This drug has a unique action. It is remarkably free from untoward effects, except for the optic nerve injury which occurs in a small percentage of patients. It is an excellent tonic, and after its administration there is usually a pronounced gain in weight and strength. Hence, it can be utilized in states of debility where it would be unwise to employ malaria or other form of fever induction. Here tryparsamid has undisputed sway and fulfils an

* Read before the Neuropsychiatry Section of the California Medical Association at the sixty-third annual session, Riverside, April 30 to May 3, 1934.

absolute indication. Its use in patients immune to malaria is indicated in that, statistically, the years of clinical trial have demonstrated the value of tryparsamid, whereas similar data for the non-malarial type of fever therapy are still forthcoming.

Whether or not tryparsamid is just as efficacious as malaria in general paresis, is an intriguing question. Statistics in this field are very difficult to compare, since the numerous variants in each series must be interpreted by each author. However, what statistics there are reveal that the results with either form of therapy are very much alike. The Wisconsin workers, who were the first to use tryparsamid clinically in 1922,[3] have recorded the largest series of cases treated with this drug alone. Reese, in his report on 317 patients for this group in October, 1933, stated [4] that the results were equally as good as those obtained with malaria. Clinical arrests or remissions were obtained in 54 per cent. The blood Wassermann test was rendered negative in 49.2 per cent. and was reduced in intensity in another 35 per cent. The spinal fluid Wassermann became negative in 25 per cent and was reduced in another 50 per cent. These results compare favorably with those established for malaria, although Moore [5] reports a larger number of serologic reversals for the malaria-treated cases. Solomon,[6] as late as 1931, states that although the question cannot be answered absolutely, he believes that the results with malaria and tryparsamid are equally good. All reports treating of the use of tryparsamid in the literature are very favorable, and I have not been able to find a single disparaging one.[7]

Statistics by Moore [8] indicate that return of the spinal fluid to normal is usually delayed until eighteen months after the malarial treatment, and that the percentage of such changes increases over a period of four more years. In three years 25 per cent of the fluids are normal, in four years 50 per cent and in five years, 75 per cent. Similarly he reports blood Wassermann reversal by malaria in 35 per cent of the cases after two years, 45 per cent after the third year, and 65 per cent after the fourth year. As stated above, it is difficult to compare these figures directly with those for tryparsamid, and the problem will never be adequately settled until a controlled series of alternate cases treated with tryparsamid and malaria is conducted. This we propose to do at the clinic of the Los Angeles County General Hospital.

The enthusiastic early reports for tryparsamid by Stokes,[9] O'Leary,[10] Moore,[11] Wile,[12] Schwab and Cady,[13] and others,[14,15,16] were not followed up subsequently. It appears that these men have adopted malaria as the treatment of choice, using tryparsamid in an auxiliary fashion or as an alternate therapy where the former cannot be utilized. Nowhere does one meet with a statement of the exact reason for this change. The impression gained from a perusal of the literature is that tryparsamid was not given up for any good and substantial reason. The danger to the optic nerve should not be responsible for this attitude, since the dangers with malaria are much greater. Furthermore, as noted a syphilologist as Moore recommends tryparsamid in the follow-up treatment of all cases which have had malaria. Since tryparsamid is being employed after malaria for the small number of additional remissions expected, estimated at from 2 to 5 per cent, the fear of optic nerve damage cannot be a serious one.

Moore and others have commented that the results with malaria plus tryparsamid are better than with either alone, and that patients not helped by the one may be benefited by the other. Kaiser and Amdur [17] cite eight cases not benefited by tryparsamid, one of which responded favorably to malaria, and fifteen cases not responding to malaria, two of which were helped with tryparsamid. One cannot say, of course, that the outcome would have been different if the original therapy was repeated or continued for a longer period. However this may be, one carries away the impression that tryparsamid produces results which may be as good as those obtained with malaria. The lesser risk and smaller expense of tryparsamid therapy, together with its greater tonic properties, would entitle tryparsamid to first place in the treatment of paresis, if this comparison with malaria could be substantiated. More work is needed on this subject.

END-RESULTS

End-points in therapy are a weighty consideration. Primarily clinical or symptomatic improvement is the most important criterion. Serologic improvement is chiefly of value because of its prognostic significance as to relapse. The generally accepted attitude is that blood Wassermann fastness is not uncommon in neurosyphilis, and is not necessarily a bad omen. The reversal of spinal fluid serology, however, is more important from the standpoint of prognosis. As mentioned previously, one must realize that serologic reversal is slow in its onset and may be progressive over a number of years after treatment has ceased. Treatment should not be stopped under the three-year period. If the spinal fluid is not normal at this time, then four out of five will not have any relapse; the relapses will occur for the greater part within five years.[18] Such patients should be observed periodically for five years, and treatment repeated if relapse occurs.

IN CONCLUSION

In conclusion, therefore, it may be stated that:

1. Spirocheticidal therapy with arsphenamin and bismuth represents a necessary adjunct to either tryparsamid or fever therapy in every case of general paresis. This treatment should follow, rather than precede, the special forms of therapy.

2. Tryparsamid is absolutely indicated in states of debility where fever therapy represents too great a hazard.

3. Tryparsamid is the treatment of choice when the patient is immune to malaria, the other forms of fever therapy being in a state of experimentation at this time.

4. Statistically, the results of tryparsamid and malarial therapy compare favorably. Should further study substantiate this, tryparsamid would be

the treatment of choice because of safety, cheapness and greater tonic properties than malaria. A controlled series of cases is desirable.

5. In the treatment of paresis, the immediate goal is clinical improvement. Serologic reversal in the spinal fluid is of value because of its prognostic significance and may be worthy of prolonged treatment. Three years of therapy, including a course of pyrexia, should be employed before treatment is discontinued in a serologic refractory case.

1930 Wilshire Boulevard.

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DISCUSSION

GEORGE S. JOHNSON, M.D. (Stanford University Hospital, San Francisco).—Doctor Ziskind has performed a distinct service in directing attention to the need of a varied approach to the problems presented by syphilis of the central nervous system. The results already obtained by the use of the agents mentioned give encouragement to continued efforts in the treatment of this condition, so long considered hopeless. It should be emphasized in relation to the use of drugs, in the late manifestations of the disease, that these tardier stages are largely preventable by proper care during the early stages. The increasing trend is to regard no patient as cured in the primary, or secondary stage, until there has been an adequate period under observation (two years), without treatment and without signs or symptoms of the presence of disease. This must necessarily include spinal-fluid examination. Continued studies along the lines indicated in this paper should do much to clarify the problems presented.

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STANLEY O. CHAMBERS, M.D. (1260 Roosevelt Building, Los Angeles). — One cannot help agree with Doctor Ziskind in his therapeutic conclusions. They are very true, and if confined to the choice of a single drug in the treatment of paresis, tryparsamid would surely represent that choice. Emphasis, however, should be placed on the toxicity of tryparsamid, for, without the utmost care and observation, optic nerve damage is constantly a threat. Optic nerve injury occurs in about 2½ per cent of cases under treatment. Repeated checking of visual fields and acuity should, therefore, be an integral part of tryparsamid therapy.

Tryparsamid, not being spirocheticidal, requires the use of arsphenamin or its derivatives in conjunction for that purpose.

Doctor Ziskind has wisely avoided the controversy existing in the field of fever therapy. Although sufficient evidence exists to assure us of its definite value, yet, as a sole specific agent, it has not held its position.

The penetrability of the central nervous system by the newer bismuth preparations has recently been questioned by the work of Klander. The therapeutic pendulum is slowly swinging back to the advisability of insoluble bismuth salts, rather than the soluble. Recent observation in my own department suggests a relation between bismuth (soluble or insoluble) and fever in the penetration of nervous-system tissues. Without fever, bismuth does not appear to penetrate the central nervous system. Yet, when fever is utilized along with the administration of bismuth, nervous-system tissues are apparently affected. If such is proved to be true, therapeutic direction in such phases of syphilis is open to a new field of principles.

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CLIFFORD W. MACK, M. D. (Livermore Sanitarium, Livermore).—The treatment of dementia paralytica by malaria or other fever-producing agents, notwithstanding the spectacular results, has not abolished the need for drug therapy. We are dealing with a generalized disease, as well as one that affects a particular organ in the body. The author rightly points out that, even after malaria, we need an agent that has not only an effect upon spirochetes in other parts of the body, but one that also has a decided constitutional effect. The arsenicals are particularly helpful in this regard, and the consensus of opinion seems to be that tryparsamid is most efficacious in neurosyphilis. The other forms of arsenic are also of value and can be used where there is danger or fear of the injurious effect of tryparsamid on the optic nerve. Also, there are instances in which malaria cannot be used because of the debilitated condition of the patient, or because the family refuses consent for such heroic measures.

It seems that the ideal method of treatment in the ordinary case is malaria or fever therapy followed by tryparsamid. The question as to which is the most suitable agent is, after all, academic rather than practical. We cannot too often point out that the patient must be treated, and not just the disease, and there may be drugs other than the heavy metals that have their place in bringing about the rehabilitation of the individual.

The author has covered the subject most thoroughly, giving us information that should be very helpful in our treatment of paresis.

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SAMUEL D. INGHAM, M.D. (1253 Roosevelt Building, Los Angeles).—The treatment of neurosyphilis in private practice offers problems different from those met with in hospitals or clinics, and a physician is often under the necessity of doing the best he can under

the existing circumstances, even when it would be better for the patient if he could be institutionalized. It is often impossible, for various reasons, to carry out malarial therapy or hyperthermia treatments, and it is, therefore, necessary to make the best compromise possible in each case. Experience of recent years has demonstrated the value of bismuth and tryparsamid for the treatment of ambulatory neurosyphilis in private practice. Some statistics indicate that results of persistent treatment, by means of the drugs now available, especially tryparsamid, compare favorably with results from malarial therapy. It is true, however, that malaria benefits some patients who are resistant to all other treatments.

CHRONIC PARANASAL SINUSITIS*

TREATMENT WITH UNDENATURED BACTERIAL ANTIGENS

By M. N. Hosmer, M.D.
San Francisco

Discussion *by William H. Strietmann, M. D., Oakland; Forest C. Kracaw, M. D., Oakland; Jau Don Ball, M. D., San Francisco.*

THE treatment of chronic sinus infections has long been a major problem in otolaryngology. Many modes of treatment have been suggested in the past, the majority of them, however, failing to meet the test of clinical trial; and most of us have been left in the position of continuing to search for some procedure which would be an improvement over previous methods.

At the present time the treatment of chronic sinusitis involves a choice between surgery and conservative medical methods. The indications for surgical treatment and the general surgical approach have been adequately defined. It will be agreed, for example, that deviated nasal septi should be straightened to provide ample drainage and ventilation; and certainly surgery is the method of choice in the management of chronic maxillary sinusitis. But I must say that in the field of ethmoidal surgery the results have not been satisfactory in a sufficiently large percentage of cases. Medical treatment—by which I mean local or topical treatment—varies with the individual physician. Minutiae of technique and medicaments have been stressed even to the point, in some instances, of obscuring principles. That a proper application of medical and surgical methods has produced good results in a majority of cases can be fairly stated. There are, however, a certain number of patients who, in spite of all sorts of treatment both surgical and medical, fail to improve. It seems to me that in these patients surgery fails to eradicate the infected tissue, and that medication of chronically infected tissue is neither logical nor productive of results. These cases present the need for immunization. Here again it is common experience that vaccine therapy directed to this end has not been uniformly successful, but it is quite possible that a large measure of the failures may lie in the type of vaccine employed. For this reason, I welcomed the opportunity to apply clinically a new type of antigen,[1] developed by Dr. A. P. Krueger of the University of California. My associates, Doctors Martin and Houston, and myself have employed Krueger's undenatured bacterial antigens in the treatment of chronic sinusitis of certain types for the past two years, and I should like to report on this group of cases.

* Read before the Northern Counties Eye, Ear, Nose and Throat Society at Sacramento, September 20, 1934.

THE UNDENATURED BACTERIAL ANTIGEN

It is Doctor Krueger's concept that the orthodox vaccine contains antigenically altered substances due to the heat and chemical treatment employed in killing the bacteria. The bacterial proteins, which represent the major immunizing fraction, have been demonstrated to be readily denatured by heat and chemical treatment. To obviate these changes, Krueger has developed a technique which, briefly, consists in:

1. Harvesting cultures grown on suitable media, in isotonic Locke's solution, and washing several times to remove metabolites.
2. Grinding in a special mechanical grinder to disrupt the cells.
3. Removal of intact cells, which escape grinding, by ultrafiltration through the acetic collodion membranes of Krueger and Ritter.[2]
4. Standardization of the filtrate on the basis of native protein content.

The filtrate consists of two components: first, a colloidal phase of bacterial fragments, and second, those unaltered constituents which have gone into true solution. The filtrate is employed without further modification for hypodermatic administration. For topical use in immunizing the paranasal mucoperiosteum, the filtrate is made up in one per cent peptone with 1 : 50,000 merthiolate. The peptone serves as a buffer for the merthiolate, and also increases the absorptive capacity of the mucous membrane.

PROCEDURE IN TREATMENT

Our cultures are taken from the infected sinuses, or from the nasal fossae, on swabs which are placed directly in plain broth and brain-broth media. From these field cultures the usual bacteriological isolation and identification are carried out. Strains of organisms, which are deemed to be pathogenic, are employed in preparing the antigen.

The immunization procedure may be divided arbitrarily, for purposes of description, into two parts, although in actual practice both are carried out simultaneously.

A. *Topical Immunization.*

The local treatment of the paranasal sinus mucoperiosteum with antigen is of primary importance. As a preliminary to it, the nasal mucous membranes are shrunken with cocain or ephedrine, and the sinuses are filled by the Proetz[3] suction displacement method. This technique, described several years ago by Proetz[3] of St. Louis, consists first in placing the patient in a recumbent position, with the head tilted well backward. Then five cubic centimeters of the antigen are instilled into each nostril and allowed to settle for a moment, after which mild suction is applied through the nares. The suction removes air from